

REMARKS

In response to the Office Action mailed May 22, 2006, Applicant has amended claims 1-3 and 9. It is urged that support for all the above amendments may be found throughout the specification as originally filed, for example at page 15, lines 1-5. No new matter has been added. The above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Claims 1-21 and 25-28 are pending in the application, with claims 13, 14 and 26 currently withdrawn due to the inclusion of non-elected species. Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks.

Applicant thanks the Examiner for noting that claims 5-8 would be allowable if rewritten in independent format.

***Claim Rejections – 35 U.S.C. § 112, second paragraph (indefiniteness)***

Claims 1-21 and 25-28 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. The Action asserts that the term "low fluence rate" is a relative term that is not defined in the claims and that is not defined in the specification in such a way that the skilled artisan can ascertain the scope of the claimed invention. The Action further asserts that claim 3 is indefinite for the recitation of "other types of fluorescent lights" and "other electroluminescent devices". Additionally, the Action asserts that it is unclear in claim 2 how the subsequent method step of "irradiating at least a portion of the subject with light at a wavelength absorbed by the photosensitizing agent" is acted upon in the case where the second conjugate comprises a prodrug which is not a photosensitizing agent.

Without acquiescing to above-noted rejections and solely to advance prosecution, Applicant has amended the claims to replace recitation of "low fluence rate" with "a rate of between about 5 and 100 mW/cm<sup>2</sup>", to remove recitation of "other" and "other types of" where applicable, and to delete recitation of prodrugs. This amendment is made without prejudice to the prosecution of any subject matter removed or modified by this amendment in a related

divisional, continuation or continuation-in-part application. Applicant respectfully submits that the rejection has been obviated and may be properly withdrawn.

***Claim Rejections – 35 U.S.C. § 112, first paragraph (enablement)***

Claims 2-12, 15-21, 27 and 28 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. In particular, the Action asserts that, while the specification is enabling with regard to a method comprising a pretargeting system for the delivery of photosensitizing agents to tumor cells in the vascular system, it allegedly does not reasonably provide enablement for a method comprising the delivery of photosensitizing agents which are prodrugs. The PTO asserts that it would require undue experimentation on the part of the skilled artisan to design synthetic strategies and produce the recited prodrugs in yields that would be adequate to use in the recited methods for treating mammalian patients.

Without acquiescing to the rejection and solely to advance prosecution, Applicant has amended the claims to remove recitation of prodrugs. This amendment is made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Applicant respectfully submits that the rejection has been obviated and may be properly withdrawn.

***Claim Rejections – 35 U.S.C. § 103***

Claims 1, 3, 4, 9-21, 25 and 28 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Richter *et al.* (U.S. Patent No. 5,484,803) in view of Schultes *et al.* (SPIE, 1994, Vol. 2078, pp 148-157), Kubler *et al.* (U.S. Patent No. 5,529,903) and Racila *et al.* (PNAS, April 1998, vol 95, pp. 4589-4594). In particular, the Action asserts that Richter *et al.* teach a method for destroying or impairing blood-borne target cells that have selectively accumulated a photosensitizing agent while leaving non-target cells relatively unimpaired by applying radiation transcutaneously. Richter *et al.* also allegedly teach the recited photosensitizing agents, wavelengths for exciting the recited photo-conjugates, durations of exposure to radiation that satisfy the limitations of the present claims 19-21, conjugation of the photosensitizing agent with an immunoglobulin, and use of the instantly recited light sources.

The Action concedes that Richter *et al.* do not specifically teach the combination of antibody conjugated photosensitizing agent and the targeting of lesions in the vascular system by antibody conjugates or the direction of light parallel to a blood vessel containing the target cells. The Action relies on Schultes *et al.*, Kubler *et al.*, and Racila *et al.* to overcome these deficiencies. The Action alleges that it would have been *prima facie* obvious at the time the claimed invention was made to combine the teachings of the cited references to arrive at Applicant's invention.

Claims 1-4, 9-12, 15-17, 19-21, 25, 27 and 28 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Richter *et al.* (U.S. Patent No. 5,484,803) in view of Schultes *et al.* (SPIE, 1994, Vol. 2078, pp 148-157), Kubler *et al.* (U.S. Patent No. 5,529,903) and Racila *et al.* (PNAS, April 1998, vol 95, pp. 4589-4594) as applied above and further in view of Theodore *et al.* (WO 95/15979). In particular, the Action asserts that it would have been obvious to the skilled artisan at the time the invention was made to combine the teachings of Theodore *et al.* on pretargeting with the other cited references to arrive at Applicant's invention of claim 2 and claims dependent therefrom.

Applicant respectfully traverses these rejections on the following grounds.

The Action fails to establish a *prima facie* case of obviousness. (*See In re Mayne*, 104 F.3d 133, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.)). The Examiner must show (1) that the combined references teach or suggest all claim limitations; (2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, a teaching, motivation, or suggestion to combine the references must exist. (*See In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

At the time of filing the present application, the cited combination of references would not have motivated a person having ordinary skill in the art to arrive at the claimed invention with the requisite reasonable expectation of success. In particular, Applicant submits that Richter *et al.* merely describe a method for destroying target cells using photosensitive

agents in blood. As admitted in the Action, nowhere does this reference teach the presently disclosed methods of targeting and pretargeting the photosensitizing agents and the targeting of lesions in the vascular system by antibody conjugates or the direction of light parallel to a blood vessel containing the target cells as recited in the instant claims. For reasons given below, the Action relies improperly on the secondary references to overcome this deficiency.

Shultes *et al.* merely describe the development of a water-soluble antibody-coupled Phthalocyanine and the use of this compound in the setting of breast cancer lesions. Shultes *et al.* fail to cure the deficiencies of Richter *et al.*, in particular by providing no actual teaching with regard to the use of targeting conjugates in methods for destroying target cells in lesions of the vascular system. Kubler *et al.* merely teach the necessity of destroying circulating cancer cells in the blood stream and Racila *et al.* teach only detecting breast cancer cells in the blood. Similarly, Theodore only generally teaches the use of a pretargeting approach for localizing photosensitizing agents. None of these references teaches destroying cells that comprise lesions of the vascular system using the claimed methods. Applicant submits that the Action employs inappropriate and selective hindsight where the allegation of obviousness is asserted to derive from a reason in the art other than knowledge provided by Applicant's disclosure. *In re Dow Chemical Co.*, 837 F.2d 469; 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). Absent the teachings of the present application, the documents cited in the Action simply fail to render the claimed invention obvious to the person having ordinary skill in the art.

In alleging that there would have been motivation to combine the references to arrive at a method for destroying or impairing target cells that comprise a lesion in the vascular system, at best, the Action asserts nothing more than that it would have been "obvious to try". Such an assertion cannot be regarded as a conclusory finding that the claimed invention is obvious, and in fact fails to support a *prima facie* case of obviousness. *In re Eli Lilly & Co.*, 902 F.2d 943; 14 USPQ2d 1741 (Fed. Cir. 1990).

Claims 1, 3, 9-12, 18-21, 25 and 28 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Abels *et al.* (WO 97/31582) in view of the abstract of Goetz *et al.* (WO 97/33620) and Schultes *et al.* (SPIE, 1994, Vol. 2078, pp.148-157). The Action asserts that Abels *et al.* teach the use of ICG for treating vascularized tumors and their metastases

comprising administering ICG followed by irradiation with light. Abels *et al.* allegedly teach the light source as recited in claim 3, low fluence rates, and the doses as recited in the instant claims. Similar to the above rejection, the Action concedes that Abels *et al.* do not teach conjugation of ICG with targeting antibodies. The Action relies on Schultes *et al.* and the abstract of Goetz *et al.* to overcome this deficiency. As such, the Action alleges that it would have been *prima facie* obvious at the time of the invention was made for the skilled artisan to combine the teachings of the cited references to arrive at Applicant's invention.

Claims 1-3, 9-12, 15-21, 25, 27 and 28 also stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Abels *et al.* (WO 97/31582) and the abstract of Goetz *et al.* (WO 97/33620) and Schultes *et al.* (SPIE, 1994, Vol. 2078, pp.148-157) as applied to claims 1, 3, 9-12, 18-21, 25 and 28 above, and further in view of Theodore *et al.* (WO 95/15979). In particular, the Action asserts that it would have been obvious to the skilled artisan at the time the invention was made to combine the teachings of Theodore *et al.* on pretargeting with the other cited references to arrive at Applicant's invention.

Applicant respectfully traverses the rejection on the following grounds.

Again, the PTO fails to establish a *prima facie* case of obviousness. (*See In re Mayne*, 104 F.3d 133, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.)). As noted above, Shultes *et al.* merely describe the development of a water-soluble antibody-coupled Phthalocyanine and the use of this compound in the setting of breast cancer lesions. Shultes *et al.* fail to cure the deficiencies of Abels *et al.*, in particular by providing no actual teaching with regard to the use of targeting conjugates in methods for destroying target cells in lesions of the vascular system. The abstract of Goetz *et al.* also fails to remedy the deficiencies of Abels *et al.* and in fact provides only a single sentence describing the use of ICG-antibody conjugates for the treatment of tumors. Similarly, and as noted previously, Theodore only generally teaches the use of a pretargeting approach for localizing photosensitizing agents. Thus, none of these references teaches destroying cells that comprise lesions of the vascular system using the claimed methods and targeting agents. Again, Applicant submits that the Action employs inappropriate and selective hindsight. In the absence

of the teachings of the present application, the documents cited in the Action simply fail to render the claimed invention obvious to the person having ordinary skill in the art.

Accordingly, Applicant submits that the primary and secondary references, taken individually or for what they teach as a whole, do not teach or suggest the claimed invention. Therefore, Applicant submits that the claimed invention would not have been obvious to the ordinarily skilled artisan at the time of filing. Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above amendments and remarks, the claims are now believed to be in condition for allowance. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at 206-622-4900 to resolve same.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



William T. Christiansen  
Registration No. 44,614

WTC/JAU:ms

701 Fifth Avenue, Suite 5400  
Seattle, Washington 98104  
Phone: (206) 622-4900  
Fax: (206) 682-6031

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